Coronary artery bypass graft (CABG) surgery has been a great advance in the treatment of coronary artery disease, but the treatment of saphenous vein bypass graft (SVBG) disease remains a frustrating challenge. Although the natural history of coronary artery disease occurs over decades, the natural history of SVBG disease occurs over years. Denudation of endothelial cells in freshly harvested saphenous veins at the time of CABG results in acute platelet and thrombin deposition that can lead to early SVBG thrombosis if there is poor flow in the graft because of surgical issues or disease in the microcirculation.\(^1\) Although the left internal mammary artery (LIMA) graft adapts well to the hemodynamic stress of coronary perfusion, the SVBG must adapt to high-pressure pulsatile arterial flow and that can contribute to chronic endothelial dysfunction. The resulting platelet and leukocyte activation can stimulate smooth muscle cell proliferation that narrows the SVBG lumen diameter. SVBG atherosclerosis, similar to coronary artery atherosclerosis, can develop later, and acute plaque rupture can cause late SVBG thrombosis.

Compared with native coronary artery atherosclerosis, SVBG atherosclerosis can be more diffuse, the fibrous cap can be weaker and thinner, and the plaque can be more fragile and friable, making it prone to distal embolization of atherosclerotic debris during percutaneous coronary intervention (PCI).\(^1\) In patients with acute SVBG thrombosis, the lack of side branches, the larger diameter of the vessel, and consequently, lower flow velocities promote excessive thrombus formation. The more distal the culprit lesion, the greater the thrombus burden in the proximal bypass conduit, and the more likely distal embolization will result in the microvascular no-reflow phenomenon with primary PCI.

Early reports on fibrinolytic therapy in patients with ST-segment–elevation myocardial infarction demonstrated lower SVBG reperfusion rates than in native coronary arteries.\(^2,3\) Similarly, primary PCI in SVBGs with balloon angioplasty or stent implantation has lower successful reperfusion rates, lower long-term patency rates, and higher complication rates, including death than in native coronary arteries.\(^4–12\) No additional SVBG reperfusion benefit has been gained with intragraft fibrinolytic therapy, intravenous platelet glycoprotein IIb/IIIa inhibitors, mechanical or aspiration thrombectomy, or distal embolic protection devices.

In this issue of *Circulation: Cardiovascular Interventions*, Iqbal et al report on 79,295 patients in the British Cardiovascular Interventions Society (BCIS) registry undergoing primary PCI in England and Wales between 2007 and 2012.\(^13\) Mean follow-up was 2.4±1.6 years. Prior CABG was present in 2658 (3.4%) patients, with the culprit vessel the bypass graft in 1490 (56%) and the native coronary artery in 1168 (44%). Patients with prior CABG had more comorbidities and higher mortality at 30 days and 1 year, but after multivariable adjustment and propensity score matching, no added risk for mortality could be attributed to history of prior CABG. Moreover, there was no impact of prior CABG on rates for reinfarction, target vessel revascularization or in-hospital mortality, major bleeding, or stroke. The authors did not report data on coronary artery lesion anatomy, procedural outcomes, or myocardial infarction size.

Similarly, Gruberg et al recently published in-hospital outcomes from the National Cardiovascular Data Registry (NCDR) on 15,628 patients undergoing primary PCI at 297 hospitals in the United States between 2009 and 2011; 969 (6%) had prior CABG.\(^14\) In these patients, the culprit vessel was the SVBG in 53.1%, the LIMA graft in 1.3%, and the native coronary artery in 45.3%. Unadjusted mortality rates were higher with prior CABG, but were not statistically different after multivariable adjustment. The adjusted mortality rate was doubled when the culprit vessel was the bypass graft compared with the native coronary artery, but was not statistically different. Also, there was no impact of prior CABG on reinfarction, stroke, or major bleeding rates.

Strengths of the BCIS study include the enrollment of every patient in England and Wales undergoing primary PCI during the study period and long-term follow-up, compared with the NCDR study that only reported hospital outcomes from participating hospitals.\(^13,14\) Both reports are notable for the large number of patients with prior CABG and the documentation of higher unadjusted mortality rates in patients with prior CABG, confirming observations from the smaller earlier reports\(^4–12\) and clinical experience. The major limitation with both reports is selection bias that excluded patients with ST-segment–elevation myocardial infarction and prior CABG who either were not referred for emergency coronary
angiography or who were excluded after coronary angiography by the interventional cardiologist who chose not to pursue primary PCI for angiographic or clinical reasons. Most importantly, both large observational registry reports leave the clinician with the misguided message that prior CABG is not an important variable in primary PCI or ST-segment–elevation myocardial infarction care. It should be noted that the investigators were evaluating a data element in a multivariable analysis, rather than evaluating patient risk for primary PCI.

Iqbal et al suggest that patients with prior CABG are unfairly being denied primary PCI because of a perceived lack of efficacy.13 However, claiming that prior CABG should not be an important variable in patient risk assessment by the interventional cardiologist misses the clinical point that these patients do represent a high-risk subgroup precisely because they are older and more often have complex multivessel coronary artery disease, prior myocardial infarction, and lower left ventricular ejection fraction.13,14 They also more frequently have hyperlipidemia, hypertension, diabetes mellitus, heart failure, peripheral artery disease, chronic lung disease, cerebrovascular disease, and end-stage renal disease on dialysis.13,14 And, from a PCI perspective, they often have a degenerated SVBG culprit lesion where primary PCI success rates are lower and no-reflow rates are higher. A more balanced conclusion on this subject was made by Al Suwaldi et al who also noted no impact of the prior CABG variable on adverse outcomes with multivariable analysis, but found higher risk for patients with prior CABG because of adverse baseline characteristics and with SVBG primary PCI.7

A reflection of primary PCI selection bias in the prior CABG subset in PCI registries was illustrated by Stone et al.8 In the Second Primary Angioplasty in Myocardial Infarction (PAMI-2) trial, 1,100 patients with ST-segment–elevation myocardial infarction underwent emergent cardiac catheterization at 34 centers; 58 (5.3%) had prior CABG, with the culprit vessel the bypass graft in 32 (55%) and the native coronary artery in 26 (45%). These cohorts are concordant with the cohort data in the BCIS and NCDR reports.13,14 However, PCI was less likely to be performed when the culprit vessel was an SVBG in a CABG patient than a native coronary artery in a non–CABG patient (71.9% versus 89.8%), and Thrombolysis in Myocardial Infarction flow grade 3 was less frequently achieved (70.2% versus 94.3%), despite selecting patients for primary PCI, with the culprit vessel the bypass graft in 32 (55%) and the native coronary artery in 26 (45%). These cohorts are concordant with the cohort data in the BCIS and NCDR reports.13,14 However, PCI was less likely to be performed when the culprit vessel was an SVBG in a CABG patient than a native coronary artery in a non–CABG patient (71.9% versus 89.8%), and Thrombolysis in Myocardial Infarction flow grade 3 was less frequently achieved (70.2% versus 94.3%), despite selecting patients for primary PCI. In-hospital and 6-month mortality rates were higher in patients with prior CABG. Similar results have subsequently been reported.10,12

Why might the results with the prior CABG variable not predict risk after multivariable analysis in an observational database limited by selection bias and unknown confounding variables? There are several possible reasons. First, the higher risk for SVBG primary PCI is diluted by including patients with prior CABG with culprit lesions in native coronary arteries where increased risk has not been found.6,12 Second, myocardial infarct size is smaller in patients with prior CABG because the saphenous vein is usually grafted to coronary artery side branches with smaller infarct artery distributions compared with the infarct artery distributions of proximal or mid-segment main artery culprit lesions.10 Third, myocardial infarct size can also be smaller if some antegrade flow is maintained in the native coronary artery with SVBG occlusion or in the SVBG with native coronary artery occlusion. Finally, because patients with prior CABG usually have a patent LIMA graft, they are more likely to have inferior myocardial infarction where mortality risk is lower. In the NCDR study, only 14.5% of patients with prior CABG had a left anterior descending infarct artery, compared with 39.8% in patients without prior CABG.14

Interventional cardiologists sometimes do not perform SVBG primary PCI when the thrombus burden is too large, the occluded SVBG perfuses a branch artery with a small myocardial distribution, or collateral flow has already been recruited. When the expected infarct size is small in a stable patient with SVBG thrombosis and significant comorbidities, and the risk of procedural complications is increased, medical therapy is sometimes the best treatment option, especially if the LIMA graft is patent and left ventricular function is preserved.

And so, despite the concordant results of 2 excellent observational reports confirming prior reports1,2 and claiming prior CABG does not confer additional risk with primary PCI, patients with prior CABG do have increased in-hospital and long-term morbidity and mortality because of more comorbidities, greater atherosclerotic disease burden, degenerating SVBGs, and worse left ventricular function and because door-to-balloon times are delayed and primary PCI success rates are lower compared with patients without prior CABG.3,10,14 In the future, hybrid revascularization with implantation of a LIMA-left anterior descending graft without full sternotomy and drug-eluting stent implantation in non–left anterior descending arteries, when possible, could greatly decrease the burden of SVBG disease on patients and interventional cardiologists.15

Disclosures

None.

References

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**Key Words:** Editorials • atherosclerosis • coronary artery bypass graft • endothelial cell • primary PCI • saphenous vein bypass graft
Misguided Use of Multivariable Analysis to Study Primary Percutaneous Coronary Intervention in Patients With Prior Coronary Artery Bypass Graft

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Circ Cardiovasc Interv. 2016;9:
doi: 10.1161/CIRCINTERVENTIONS.116.003884

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